A ONE-STEP TRANSFORMATION OF (*S*)-1-BENZOYL-3-[(*E*)-DIMETHYLAMINOMETHYLIDENE]-5-METHOXYCARBONYL-PYRROLIDIN-2-ONE INTO QUINOLIZINYL- AND 2*H*-2-PYRANONYL-SUBSTITUTED ALANINE DERIVATIVES

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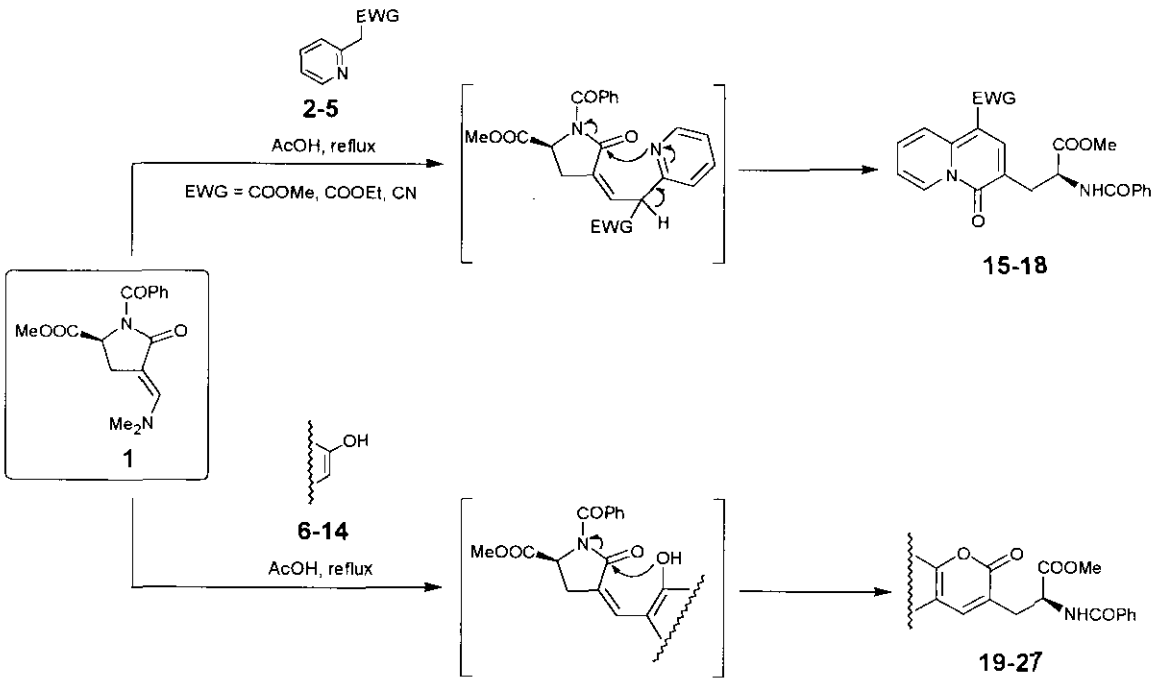
Abstract - (*S*)-1-Benzoyl-3-[(*E*)-dimethylaminomethylidene]-5-methoxycarbonylpyrrolidin-2-one (**1**) was transformed in one step with various 1,3-dinucleophiles (**2-14**) into the corresponding *N*-benzoyl-3-quinolizinyl- (**15-18**) and *N*-benzoyl-3-(2*H*-2-pyranonyl)alanine methyl esters (**19-27**).

Due to their occurrence in nature, biological activity, and synthetic utility, there has been in the last few decades a significant interest for the synthesis of 3-heteroarylalanines.[1] Among various synthetic approaches, transformations of commercially available α-amino acids, such as serine, aspartic acid, and glutamic acid, are often used for the preparation of 3-heteroarylalanines.[2] Among them, only few preparations of pyranonylalanines have been reported.[3] Recently, Young and coworkers reported on the synthesis of 3-pyrazolyl-, 3-isoxazolyl-, and 3-pyrimidinylalanines from (*S*)-3-formylpyroglutamic acid derivatives, using a 'ring switching' strategy.[4] On the other hand, we have previously shown that 3-dimethylaminopropenoates can serve as versatile reagents for the preparation of a variety of heterocyclic systems.[5-7] In continuation of our work in this field, we report on efficient, one step synthesis of novel *N*-benzoyl-3-heteroarylalanine esters (**15-27**) from easily available (*S*)-1-benzoyl-3-[(*E*)-dimethylaminomethylidene]-5-methoxycarbonylpyrrolidin-2-one (**1**) and by using an improved 'ring switching' strategy.

The starting compound, (*S*)-1-benzoyl-3-[(*E*)-dimethylaminomethylidene]-5-methoxycarbonyl-pyrrolidin-2-one (**1**), was prepared from L-pyroglutamic acid in three steps according to the procedure described previously.[7] This was then treated with two types of 1,3-dinucleophiles: 2-(pyridinyl-2)acetic acid derivatives (**2-5**) and carbocyclic and heterocyclic 1,3-dicarbonyl compounds and their analogs (**6-14**). Treatment of **1** with *C,N*-dinucleophiles (**2-5**) afforded quinolizinyl substituted alanine esters (**15-18**),

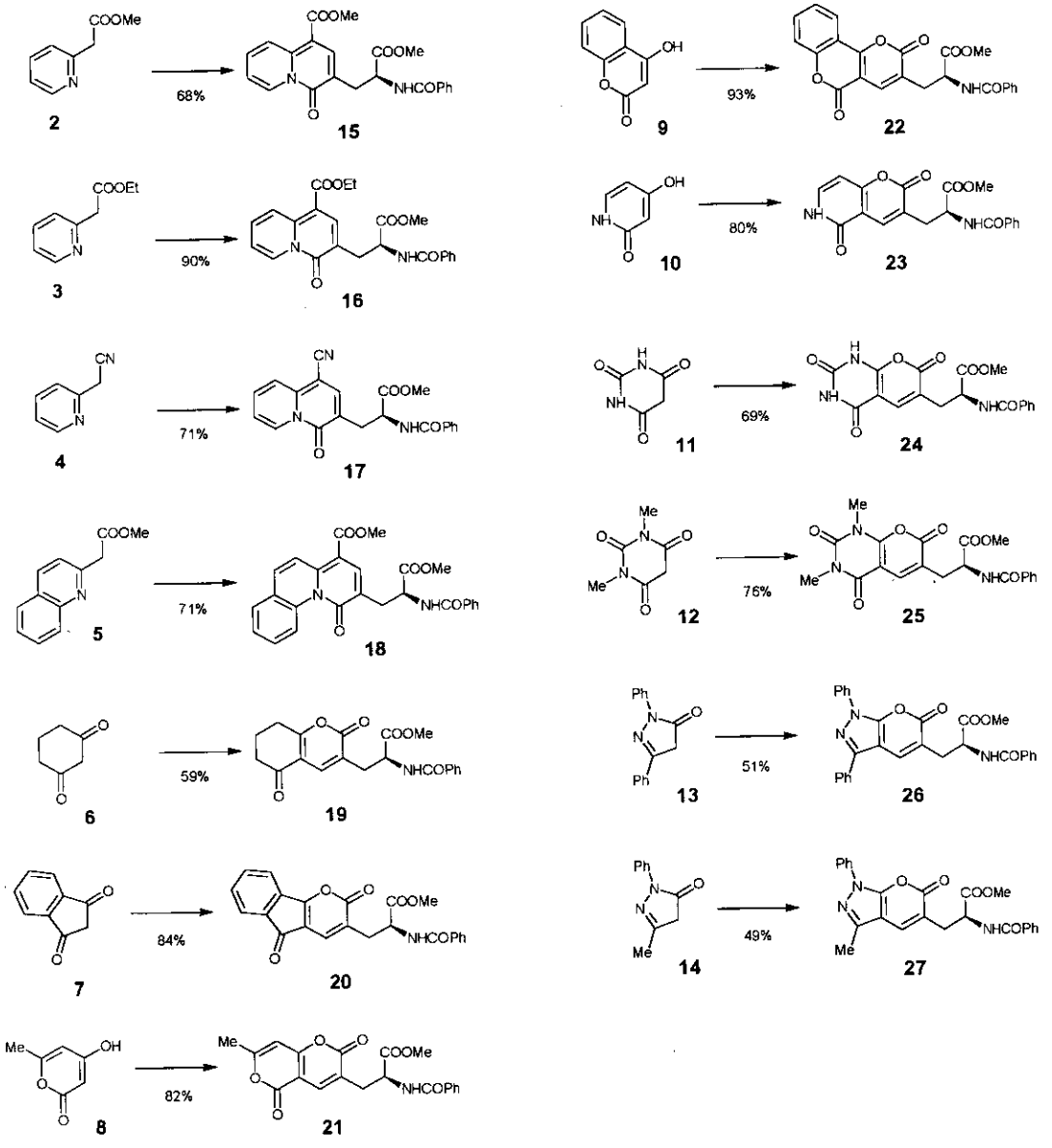
while with *C,O*-dinucleophiles (**6-14**), 3-heteroarylalanines (**19-27**) with fused 2*H*-pyran-2-one heterocyclic residue were formed (Scheme 1).

Scheme 1



Thus, methyl 2-(pyridinyl-2)acetate (**2**), ethyl 2-(pyridinyl-2)acetate (**3**), 2-(pyridinyl-2)acetonitrile (**4**), methyl 2-(quinolinyl-2)acetate (**5**), cyclohexane-1,3-dione (**6**), indane-1,3-dione (7), 4-hydroxy-6-methyl-2*H*-pyran-2-one (**8**), 4-hydroxy-2*H*-benzo[*b*]pyran-2-one (**9**), 2,4-dihydroxypyridine (**10**), barbituric acid (**11**), 1,3-dimethylbarbituric acid (**12**), 1,3-diphenyl-1*H*,4*H*-pyrazol-5-one (**13**), and 3-methyl-1-phenyl-1*H*,4*H*-pyrazol-5-one (**14**) furnished, after treatment with **1** in refluxing acetic acid, the corresponding (*S*)-*N*-benzoyl-3-heteroarylalanine methyl esters with the following heteroaryl residues, 1-methoxycarbonyl-4-oxo-4*H*-quinolizinyl-3 (**15**), 1-ethoxycarbonyl-4-oxo-4*H*-quinolizinyl-3 (**16**), 1-cyano-4-oxo-4*H*-quinolizinyl-3 (**17**), 1-methocycarbonyl-4-oxo-4*H*-benzo[*c*]quinolizinyl-3 (**18**), 2,5-dioxo-5,6,7,8-tetrahydro-2*H*-benzo[*b*]pyranyl-3 (**19**), 2,5-dioxo-2*H*,5*H*-indeno[1,2-*b*]pyranyl-3 (**20**), 2,5-dioxo-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyranyl-3 (**21**), 2,5-dioxo-2*H*,5*H*-benzo[*b*]pyrano[4,3-*b*]pyranyl-3 (**22**), 2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridinyl-3 (**23**), 2,4,7-trioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]pyrimidinyl-6 (**24**), 1,3-dimethyl-2,4,7-trioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]-pyrimidinyl-6 (**25**), 1,3-diphenyl-6-oxo-1*H*,6*H*-pyrano[2,3-*c*]pyrazolyl-5 (**26**), and 3-methyl-1-phenyl-6-oxo-1*H*,6*H*-pyrano[2,3-*c*]pyrazolyl-5 (**27**), respectively (Scheme 2).

Scheme 2



EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The ^1H NMR spectra and ^{13}C NMR spectra were obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer with DMSO-d_6 and $CDCl_3$ as solvents and Me_4Si as internal standard. The microanalyses for C, H, and N were obtained on a Perkin-Elmer CHN *Anal*yser 2400. The optical rotations were measured on a Perkin-Elmer 241 MC Polarimeter.

(*S*)-1-Benzoyl-3-[(*E*)-dimethylaminomethylidene]-5-methoxycarbonylpyrrolidin-2-one (**1**) was prepared according to the procedure described in the literature.[7]

General Procedure for the Preparation of (*S*)-*N*-Benzoyl-3-heteroarylalanine methyl esters (15-27): A mixture of (*S*)-1-benzoyl-3-[(*E*)-dimethylaminomethylidene]-5-methoxycarbonylpyrrolidin-2-one (**1**) (1 mmol), 1,3-dinucleophile (**2-14**) (1 mmol), and glacial acetic acid (4 mL) was heated at reflux temperature for 2-5 h. Volatile components were evaporated *in vacuo*, the solid residue crystallised from methanol, and the precipitate collected by filtration to give *N*-benzoyl-3-heteroarylalanine methyl ester (**15-27**).

(*S*)-*N*-Benzoyl-3-(1-methoxycarbonyl-4-oxo-4*H*-quinolizinyl-3)alanine methyl ester (15). This compound was prepared from methyl 2-(pyridinyl-2)acetate (**2**), reflux for 2 h; yield 68%; mp 223-225°C (from methanol); $[\alpha]_D^{23}$ = +35.8° (*c* = 0.84, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.05 (1H, dd, *J* = 9.8, 13.4 Hz, 3-Ha), 3.35 (1H, dd, *J* = 4.8, 13.5 Hz, 3-Hb), 3.66 (3H, s, OMe), 3.80 (3H, s, OMe), 4.81 (1H, ddd, *J* = 4.8, 7.9, 9.7 Hz, 2-H), 7.43-7.53 (4H, m, 3H-Ph 7'-H), 7.76-7.79 (2H, m, 2H-Ph), 7 88-7.89 (1H, m, 8'-H), 8.39 (1H, s, 2'-H), 8.85 (1H, d, *J* = 7.8 Hz, NH), 9.05 (1H, d, *J* = 9.1 Hz, 9'-H), 9.22 (1H, d, *J* = 7.1 Hz, 6'-H). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 33.3, 52.6, 52.6, 52.9, 101.2, 115.4, 118.0, 123.9, 128.1, 128.9, 129.1, 132.3, 134.6, 135.1, 141.1, 144.2, 158.7, 165.8, 167.4, 172.9. *Anal.* Calcd for $C_{22}H_{20}N_2O_6$: C, 64.70; H, 4.94; N, 6.86. Found: C, 64.60; H, 4.80; N, 6.78.

(*S*)-*N*-Benzoyl-3-(1-ethoxycarbonyl-4-oxo-4*H*-quinolizinyl-3)alanine methyl ester (16). This compound was prepared from ethyl 2-(pyridinyl-2)acetate (**3**), reflux for 3 h; yield 90%; mp 207-209°C (from methanol); $[\alpha]_D^{23}$ = +27.2° (*c* = 1.12, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.28 (3H, t, *J* = 7.2 Hz, CH_3CH_2), 3.05 (1H, dd, *J* = 10.0, 13.4 Hz, 3-Ha), 3.36 (1H, dd, *J* = 4.5, 13.6 Hz, 3-Hb), 3.67 (3H, s, OMe), 4.26 (2H, q, *J* = 7.2, CH_2CH_3), 4.79 (1H, ddd, *J* = 4.9, 7.9, 9.8 Hz, 2-H), 7.40-7.47 (3H, m, 3H-Ph), 7.50-7.56 (1H, m, 7'-H), 7.77-7.80 (2H, m, 2H-Ph), 7.87 (1H, ddd, *J* = 1.5, 6.8, 9.4 Hz, 8'-H), 8.40 (1H, s, 2'-H), 8.88 (1H, d, *J* = 7.9 Hz, NH), 9.06 (1H, dt, *J* = 1.1, 9.4 Hz, 9'-H), 9.22 (1H, dt, *J* = 1.1, 7.5 Hz, 6'-H). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 15.0, 33.2, 52.6, 52.9, 61.2, 101.5, 115.4, 117.9, 123.9, 128.1, 128.9, 129.1, 132.3, 134.6, 135.0, 141.0, 144.2, 158.7, 165.4, 167.3, 172.8. *Anal.* Calcd for $C_{23}H_{22}N_2O_6$: C, 65.39; H, 5.25; N, 6.63. Found: C, 65.20; H, 5.42; N, 6.55.

(*S*)-*N*-Benzoyl-3-(1-cyano-4-oxo-4*H*-quinolizinyl-3)alanine methyl ester (17). This compound was prepared from 2-(pyridinyl-2)acetonitrile (**4**), reflux for 3 h; yield 71%; mp 231-233°C (from methanol); $[\alpha]_D^{23}$ = –2.5° (*c* = 1.01, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.04 (1H, dd, *J* = 9.8, 13.6 Hz, 3-Ha),

3.30 (1H, dd, J = 5.1, 13.4 Hz, 3-Hb), 3.66 (3H, s, OMe), 4.84 (1H, ddd, J = 5.1, 7.7, 9.8 Hz, 2-H), 7.43-7.56 (4H, m, 3H-Ph and 7'-H), 7.77-7.80 (2H, m, 2H-Ph), 7 .90-7.93 (2H, m, 8'-H and NH), 8.07 (1H, s, 2'-H), 8.80 (1H, d, J = 7.9 Hz, 9'-H), 9.16 (1H, dt, J = 1.0, 7.2 Hz, 6'-H). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 32.3, 51.4, 52.0, 82.8, 116.4, 117.2, 117.6, 122.6, 127.2, 128.2, 128.3, 131.5, 133.6, 135.2, 139.8, 144.5, 157.2, 166.5, 171.9. *Anal.* Calcd for $C_{21}H_{17}N_3O_4$: C, 67.19; H, 4.56; N, 11.19. Found: C, 67.16; H, 4.78; N, 11.24.

(*S*)-*N*-Benzoyl-3-(1-methocycarbonyl-4-oxo-4*H*-benzo[*c*]quinolizinyl-3)alanine methyl ester (18). This compound was prepared from methyl 2-(quinolinyl-2)acetate (**5**), reflux for 3 h; yield 71%; mp 245-246°C (from methanol); $[\alpha]_D^{23}$ = +44.1° (c = 0.99, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.04 (1H, dd, J = 10.2, 13.6 Hz, 3-Ha), 3.36 (1H, dd, J = 4.9, 13.2 Hz, 3-Hb), 3.68 (3H, s, OMe), 3.79 (3H, s, OMe), 4.91 (1H, ddd, J = 4.5, 8.3, 9.4 Hz, 2-H), 7.42-7.58 (3H, m, 3H-Ph), 7.60-7.67 (2H, m, 7'-H, 8'-H), 7.76-7.79 (2H, m, 2H-Ph), 7.86 (1H, dd, J = 2.1, 7.4 Hz, 9'-H), 7.90 (1H, d, J = 9.4 Hz, 10'-H), 8.15 (1H, s, 2'-H), 8.63 (1H, d, J = 9.8 Hz, 11'-H), 8.83 (1H, d, J = 7.9 Hz, NH), 9.36 (1H, dd, J = 1.1, 7.9 Hz, 6'-H). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 33.8, 52.1, 52.9, 52.9, 104.4, 120.9, 122.7, 123.2, 126.3, 127.2, 128.0, 128.1, 128.8, 129.1, 129.5, 132.3, 133.9, 134.7, 138.9, 144.6, 164.2, 166.1, 167.4, 172.8. *Anal.* Calcd for $C_{26}H_{22}N_2O_6$: C, 68.12; H, 4.84; N, 6.11. Found: C, 68.05; H, 4.88; N, 6.29.

(*S*)-*N*-Benzoyl-3-(2,5-dioxo-5,6,7,8-tetrahydro-2*H*-benzo[*b*]pyranyl-3)alanine methyl ester (19). This compound was prepared from cyclohexane-1,3-dione (**6**), reflux for 3 h; yield 59%; mp 185-188°C (from methanol); $[\alpha]_D^{23}$ = +2.6° (c = 0.78, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.02 (2H, deg tt, J = 6.3, 6.3 Hz, 7'-CH_2), 2.44 (2H, t, J = 6.6 Hz, 6'-CH_2), 2.83 (2H, t, J = 6.6 Hz, 8'-CH_2), 2.87 (1H, dd, J = 10.2, 14.3 Hz, 3-Ha), 3.06 (1H, dd, J = 4.9, 14.3 Hz, 3-Hb), 3.66 (3H, s, OMe), 4.76 (1H, ddd, J = 4.7, 8.1, 10.2 Hz, 2-H), 7.43-7.57 (3H, m, 3H-Ph), 7.73 (1H, s, 4'-H), 7.77-7.81 (2H, m, 2H-Ph), 8.77 (1H, d, J = 8.3 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 19.7, 27.1, 31.7, 35.9, 50.7, 52.1, 113.7, 121.8, 127.2, 128.3, 131.6, 133.5, 137.2, 160.7, 166.8, 171.6, 173.8, 194.2. *Anal.* Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.18; N, 3.79. Found: C, 64.92; H, 5.35; N, 3.87.

(*S*)-*N*-Benzoyl-3-(2,5-dioxo-2*H*,5*H*-indeno[1,2-*b*]pyranyl-3)alanine methyl ester (20). This compound was prepared from indane-1,3-dione (**7**), reflux for 3 h; yield 84%; mp 151-153°C (from methanol); $[\alpha]_D^{23}$ = –21.0° (c = 1.01, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.92 (1H, dd, J = 10.2, 13.9 Hz, 3-Ha), 3.12 (1H, dd, J = 4.8, 13.7 Hz, 3-Hb), 3.69 (3H, s, OMe), 4.82 (1H, ddd, J = 4.9, 8.1, 10.0 Hz, 2-H), 7.43-7.64 (8H, m, 3H-Ph and 5H-Het), 7.78-7.81 (2H, m, 2H-Ph), 8.79 (1H, d, J = 8.3 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 33.5, 51.6, 53.0, 111.5, 121.1, 122.3, 124.2, 128.1, 129.2, 132.5, 133.0, 133.4, 134.4, 135.2,

135.9, 136.2, 161.6, 167.6, 172.4, 175.3, 188.3. *Anal.* Calcd for $C_{23}H_{17}NO_6$: C, 68.48; H, 4.25; N, 3.47. Found: C, 68.50; H, 4.28; N, 3.63.

(*S*)-*N*-Benzoyl-3-(2,5-dioxo-7-methyl-2*H*,5*H*-pyrano[4,3-*b*]pyranyl-3)alanine methyl ester (21). This compound was prepared from 4-hydroxy-6-methyl-2*H*-pyran-2-one (**8**), reflux for 2 h; yield 82%; mp 220-222°C; $[\alpha]_D^{23} = -21.3°$ (c = 0.77, $CHCl_3$). ^1H NMR (300 MHz, DMSO-d_6): δ 2.30 (3H, s, 7-Me), 2.91 (1H, dd, J = 10.2, 13.9 Hz, 3-Ha), 3.11 (1H, dd, J = 4.5, 13.9 Hz, 3-Hb), 3.68 (3H, s, OMe), 4.79 (1H, ddd, J = 4.9, 7.9, 10.2 Hz, 2-H), 6.63 (1H, s, 8'-H), 7.43-7.56 (3H, m, 3H-Ph), 7.76-7.80 (3H, m, 2H-Ph and 4'-H), 8.78 (1H, d, J = 7.9 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 19.8, 32.0, 50.7, 52.1, 98.7, 100.8, 122.5, 127.2, 128.3, 131.5, 133.6, 137.8, 159.5, 159.8, 164.8, 165.7, 166.6, 171.5. *Anal.* Calcd for $C_{20}H_{17}NO_7$: C, 62.66; H, 4.47; N, 3.65. Found: C, 62.29; H, 4.51; N, 3.45.

(*S*)-*N*-Benzoyl-3-(2,5-dioxo-2*H*,5*H*-benzo[*b*]pyrano[4,3-*b*]pyranyl-3)alanine methyl ester (22). This compound was prepared from 4-hydroxy-2*H*-benzo[*b*]pyran-2-one (**9**), reflux for 2 h; yield 93%; mp 220-222°C (from methanol); $[\alpha]_D^{23} = -52.6°$ (c = 0.88, $CHCl_3$). ^1H NMR (300 MHz, DMSO-d_6): δ 3.00 (1H, dd, J = 10.1, 13.9 Hz, 3-Ha), 3.18 (1H, dd, J = 4.6, 13.9 Hz, 3-Hb), 3.70 (3H, s, OMe), 4.85 (1H, ddd, J = 4.9, 7.9, 10.1 Hz, 2-H), 7.45-7.54 (5H, m, 3H-Ph, 8'-H, 9'-H), 7.77-7.81 (3H, m, 2H-Ph, 7'-H), 7.93 (1H, s, 4'-H), 8.00 (1H, dd, J = 1.0, 6.7 Hz, 10'-H), 8.82 (1H, d, J = 8.0 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 33.0, 51.6, 53.1, 104.3, 113.7, 118.0, 123.8, 125.5, 126.2, 128.2, 129.2, 132.4, 134.5, 135.2, 139.0, 153.6, 159.3, 160.0, 160.8, 167.6, 172.4. *Anal.* Calcd for $C_{23}H_{17}NO_7$: C, 65.87; H, 4.09; N, 3.34. Found: C, 65.77; H, 4.05; N, 3.34.

(*S*)-*N*-Benzoyl-3-(2,5-dioxo-5,6-dihydro-2*H*-pyrano[3,2-*c*]pyridinyl-3)alanine methyl ester (23). This compound was prepared from 2,4-dihydroxypyridine (**10**), reflux for 2 h; yield 80%; mp 276-279°C (from DMF/methanol); $[\alpha]_D^{23} = -62.9°$ (c = 1.12, DMF). ^1H NMR (300 MHz, DMSO-d_6): δ-ppm: 2.91 (1H, dd, J = 10.2, 14.0 Hz, 3-Ha), 3.12 (1H, dd, J = 4.7, 13.8 Hz, 3-Hb), 3.67 (3H, s, OMe), 4.80 (1H, ddd, J = 4.5, 7.9, 9.8 Hz, 2-H), 6.33 (1H, d, J = 7.2, 8'-H), 7.43-7.58 (4H, m, 3H-Ph and 7'-H), 7.77-7.80 (2H, m, 2H-Ph), 7.88 (1H, s, 4'-H), 8.79 (1H, d, J =7.9 Hz, NH), 11.91 (1H, s, 6'-H). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 32.1, 50.8, 52.0, 97.3, 108.0, 121.4, 127.2, 128.2, 131.4, 133.6, 138.0, 138.1, 159.8, 160.2, 162.5, 166.5, 171.6. *Anal.* Calcd for $C_{19}H_{16}N_2O_6$: C, 61.96; H, 4.38; N, 7.61. Found: C, 61.66; H, 4.43; N, 7.52.

(*S*)-*N*-Benzoyl-3-(2,4,7-trioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]pyrimidinyl-6)alanine methyl ester (24). This compound was prepared from barbituric acid (**11**), reflux for 5 h; yield 69%; mp 273-275°C (from

methanol); $[\alpha]_D^{23}$ = –107.6° (*c* = 0.68, DMF). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.84 (1H, dd, *J* = 10.2, 14.0 Hz, 3-Ha), 3.02 (1H, dd, *J* = 4.7, 13.7 Hz, 3-Hb), 3.67 (3H, s, OMe), 4.74 (1H, ddd, *J* = 4.7, 8.1, 9.8 Hz, 2-H), 7.43-7.57 (3H, m, 3H-Ph), 7.75 (1H, s, 4'-H), 7.78-7.81 (2H, m, 2H-Ph), 8.25 (1H, br s, NH), 8.74 (1H, d, *J* = 8.3 Hz, NH), 11.26 (1H, s, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 31.5, 50.9, 52.1, 91.7, 114.6, 127.2, 128.3, 131.5, 133.6, 139.4, 148.9, 158.8, 159.3, 160.4, 166.7, 171.6. *Anal.* Calcd for $C_{18}H_{15}N_3O_7$: C, 56.11; H, 3.92; N, 10.90. Found: C, 55.90; H, 3.90; N, 10.89.

(*S*)-*N*-Benzoyl-3-(1,3-dimethyl-2,4,7-trioxo-1,2,3,4-tetrahydro-7*H*-pyrano[2,3-*d*]-pyrimidinyl-6)alanine methyl ester (25). This compound was prepared from 1,3-dimethylbarbituric acid (**12**), reflux for 3 h; yield 76%; mp 218-220°C (from methanol); $[\alpha]_D^{23}$ = –40.0° (*c* = 0.78, CH_2Cl_2). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.90 (1H, dd, *J* = 10.2, 14.0 Hz, 3-Ha), 3.07 (1H, dd, *J* = 4.5, 13.9 Hz, 3-Hb), 3.20 (3H, s, N-Me), 3.37 (3H, s, N-Me), 3.78 (3H, s, OMe), 4.77 (1H, ddd, *J* = 4.7, 8.1, 10.2 Hz, 2-H), 7.43-7.57 (3H, m, 3H-Ph), 7.79-7.82 (2H, m, 2H-Ph), 7.93 (1H, s, 4'-H); 8.77 (1H, d, *J* = 7.9 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 28.8, 29.7, 32.2, 51.8, 53.0, 92.9, 115.1, 128.2, 129.2, 132.4, 134.5, 141.3, 150.2, 158.5, 159.3, 159.6, 167.5, 172.6. *Anal.* Calcd for $C_{20}H_{19}N_3O_7$: C, 58.11; H, 4.63; N, 10.16. Found: C, 58.10; H, 4.69; N, 10.20.

(*S*)-*N*-Benzoyl-3-(1,3-diphenyl-6-oxo-1*H*,6*H*-pyrano[2,3-*c*]pyrazolyl-5)alanine methyl ester (26). This compound was prepared from 1,3-diphenyl-1*H*,4*H*-pyrazol-5-one (**13**), reflux for 3 h; yield 51%; mp 208-210°C (from methanol); $[\alpha]_D^{23}$ = +20.6° (*c* = 0.95, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.97 (1H, dd, *J* = 10.4, 13.7 Hz, 3-Ha), 3.17 (1H, dd, *J* = 4.9, 13.4 Hz, 3-Hb), 3.70 (3H, s, OMe), 4.81 (1H, ddd, *J* = 4.7, 8.1, 10.0 Hz, 2-H), 7.38-7.54 (7H, m, 7H-Ph), 7.59-7.65 (2H, m, 2H-Ph), 7.80-7.84 (4H, m, 4H-Ph), 7.87-7.90 (2H, m, 2H-Ph), 8.32 (1H, s, 4'-H), 8.82 (1H, d, *J* = 8.0 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 33.3, 52.0, 53.0, 100.5, 117.1, 121.8, 127.6, 128.2, 128.5, 129.1, 129.9, 130.1, 130.5, 132.2, 132.4, 134.5, 137.3, 139.1, 145.8, 151.0, 160.1, 167.5, 172.6. *Anal.* Calcd for $C_{29}H_{23}N_3O_5$: C, 70.58; H, 4.70; N, 8.51. Found: : C, 70.21; H, 4.93; N, 8.42.

(*S*)-*N*-Benzoyl-3-(3-methyl-1-phenyl-6-oxo-1*H*,6*H*-pyrano[2,3-*c*]pyrazolyl-5)alanine methyl ester (27). This compound was prepared from 3-methyl-1-phenyl-1*H*,4*H*-pyrazol-5-one (**14**), reflux for 3 h; yield 49%; mp 130-132°C (from methanol); $[\alpha]_D^{23}$ = +54.3° (*c* = 0.75, $CHCl_3$). ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.31 (3H, s, 3'-Me), 2.91 (1H, dd, *J* = 9.4, 13.9 Hz, 3-Ha), 3.10 (1H, dd, *J* = 4.9, 13.9 Hz, 3-Hb), 3.67 (3H, s, OMe), 4.76 (1H, ddd, *J* = 5.4, 7.7, 9.6 Hz, 2-H), 7.37-7.60 (6H, m, 6H-Ph), 7 .76-7.81 (4H, m, 4H-Ph), 7.95 (1H, s, 4'-H), 8.78 (1H, d, *J* = 7.6 Hz, NH). ^{13}C NMR (75.5 MHz, DMSO-d_6): δ 12.2, 33.6, 52.1, 53.0, 82.3,

102.1, 115.7, 121.2, 128.1, 129.2, 130.5, 132.5, 134.5, 137.3, 138.7, 145.1, 150.3, 160.6, 167.7, 172.6. *Anal.* Calcd for $C_{24}H_{21}N_3O_5$: C, 66.81; H, 4.91; N, 9.74. Found: C, 66.58; H, 5.06; N, 9.57.

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